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Mice Lacking a *Myc* Enhancer That Includes Human SNP rs6983267 Are Resistant to Intestinal Tumors

Summary:

In a study, published in Science, group have investigated a gene region that contains a particular single nucleotide variant associated with increased risk for developing colorectal and prostate cancers - and found that removing this region caused dramatic resistance to tumour formation. They had shown that the 'switches' that regulate the expression of genes play a major role in the development of cancer. Genome-wide association studies have revealed genomic regions associated with more than 200 diseases, including heart disease, diabetes and different types of cancer. However, the mechanisms by which these genomic regions act are not fully understood. One suggestion that has generated considerable interest is the possibilities that the risk polymorphisms located far from genes could function as gene regulatory elements or 'switches' that regulate expression of genes.

In the current study, which was conducted in mice, scientists have analyzed one particular single nucleotide variant in a region associated with increased risk for developing colorectal and prostate cancers, but whose mechanism of action has been unclear. Although this variant increases cancer risk only by 20 per cent, it is very common and therefore accounts for more inherited cancer than any other currently known genetic variant or mutation.

Article

Mice Lacking a *Myc* Enhancer That Includes Human SNP rs6983267 Are Resistant to Intestinal Tumors

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Abstract:

Genome wide association (GWA) studies have identified polymorphisms upstream of the *MYC* gene that are associated with increased risk for multiple different cancer types (e.g., breast (1), bladder (2), prostate (3), and colon (4)). Several lines of evidence suggest that the identified polymorphisms affect function or expression of the *MYC* oncogene.Multiple cancer-associated single nucleotide polymorphisms (SNPs) have been mapped to conserved sequences within a 500-kilobase region upstream of the MYC oncogene on human chromosome 8q24. These SNPs may affect cancer development through altered regulation of MYC expression, but this hypothesis has been difficult to confirm.

The group generated mice deficient in Myc-335, a putative MYC regulatory element that contains rs6983267, a SNP accounting for more human cancer related morbidity than any other genetic variant or mutation. In Myc-335 null mice, Myc transcripts were expressed in the intestinal crypts in a pattern similar to that in wild-type mice but at modestly reduced levels. The mutant mice displayed no overt phenotype but were markedly resistant to intestinal tumorigenesis induced by the APCmin mutation.

These results establish that a cancer associated SNP identified in GWA studies has a functional effect in vivo.

References:

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